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De novo pyrimidine synthesis is necessary for intestinal colonization of *Salmonella Typhimurium* in chicks

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Abstract

© 2017 Yang et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. *pyrE* (STM3733) encodes orotate phosphoribosyltransferase (OPRTase; EC 2.4.2.10), the fifth enzyme of the de novo pyrimidine biosynthetic pathway. We identified a Δ *pyrE* mutant as under selection in screening of a *Salmonella* mutant library in 4-day old chicks. Here, we confirm that a Δ *pyrE* mutant colonizes 4-day old chicks poorly in competitive infection with isogenic wild type, and that the ability of this mutant to colonize chicks could be restored by providing a copy of *pyrE* in trans. We further show that our Δ *pyrE* mutant grows poorly in nutrient poor conditions in vitro, and that the ability of this mutant to grow is restored, both in vitro and in chicks, when precursors to the pyrimidine salvage pathway were provided. This finding suggests that the environment in the chick intestine during our infections lacks sufficient precursors of the pyrimidine salvage pathway to support *Salmonella* growth. Finally, we show that the colonization defect of a Δ *pyrE* mutant during infection occurs in to chicks, but not in CBA/J mice or ligated ileal loops in calves. Our data suggest that de novo pyrimidine synthesis is necessary for colonization of *Salmonella Typhimurium* in the chick, and that the salvage pathway is not used in this niche.

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